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COMPARATIVE STUDY OF CONVENTIONAL URINE CYTOLOGY VERSUS THE PARIS SYSTEM WITH HISTOLOGIC CORRELATION : A SINGLE INSTITUTIONAL STUDY OF 120 CASES.

Pathology

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ABSTRACT

Background: Urine cytology continues to be an important test for screening,diagnosis and monitoring of patient with urothelial carcinoma.It is more specific for High grade urothelial cancers(HGUC) .Our objective is to compare the performance of The Paris System for Reporting Urine Cytology with our institutional reporting system.

Materials and Methods : A cross sectional observational study was conducted over a period of one year from June 2018 to May 2019. A total of 315 urine specimen was studied from 120 patients who presented with hematuria and other urinary tract symptoms to the Department of Urology. Cytological diagnosis was done by both The Paris System(TPS) and original institutional reporting system(ORS) and correlated with gold standard histology.

Results and Observation: More cases were found to be under Negative for High Grade Urothelial Carcinoma (NHGUC) i.e. 37% by TPS VS 23% by ORS, lower number of cases assigned as atypical category (AUC) using TPS (25% by TPS VS 39% by ORS),with regards to AUC category 56% cases were subsequently diagnosed as HGUC using TPS compared to 26% by institutional reposting system. There was minimal difference in performance of suspicious for high grade urothelial carcinoma (SHGUC) / high grade urothelial carcinoma (HGUC) using both the system .

Conclusion: The Paris System of reporting urine cytology has improved the performance of urine cytology by targeting the diagnosis of HGUC which is clinically significant.

KEYWORDS

urine cytology , the Paris System for reporting urine cytology, urothelial carcinoma

INTRODUCTION-

Urinary bladder cancer is the 10th most common form of cancer worldwide.It is estimated that 3 % of all new cancer cases amounting to more than half million are urinary bladder cancer and more than 200,000 cases fall under bladder cancer related mortality. It is the sixth most common cancer and ninth leading cause of cancer death in male population.(1) Urine cytology gained popularity in 1945 when Dr. George Papanicolaou and Victor F Marshall published their original article describing the use of urine cytology for detection of cancer cells .(2) Since then multiple reporting systems have been proposed but none have got universal acceptance due to lack of defined diagnostic criteria for each category. (3)The Paris system for reporting urine cytology (TPS) started in 2013 in International Congress of Cytology held in Paris and has emerged as a significant reporting system focusing on detection of high grade urothelial carcinoma (HGUC) .(4) Urine cytology remained an essential tool for screening, diagnosis and follow up of urothelial carcinoma cases despite development of ancilliary tests. It is a safe,simple, cost effective and non- invasive test which samples the entire urinary tract .(5)

MATERIALS AND METHODS-

A total of 315 urine specimen from 120 patients were evaluated from June 2018 to May 2019 at our institution averaging 2.6 samples for each patient . Centrifugation of samples were done immediately at 2000 rpm for 15 minutes to avoid degeneration and smears were prepared with Papancolaou and May-Grunwald-Giemsa stain. Cytological diagnosis was done according to our institutional reporting system and subsequently reclassified according to TPS. Histological follow up was done in each case within a period of six months from cytological diagnosis. Histologic categories were divided into benign ,low grade urothelial neoplasm (LGUN) and HGUC- which included infiltrative urothelial carcinoma,high grade papillary urothelial carcinoma and carcinoma in situ.

RESULTS-

The median age of the cases was 57.83 years with male comprising 80% (n= 96) and female comprising 20%% (n=24) . The male :female ratio is 4:1. Seventy two (80%) specimen were voided, 35% (n=42) were catheterised and 5% were bladder wash samples. Most patients (85 % ,n=102) presented with complain of hematuria ,either alone or with associated irritative symptoms. The cytological diagnosis by ORS had 23% negative for malignancy,39% AUC,17% suspicious for malignancy , 20% positive for malignancy and diagnosis by TPS had 37% NHGUC, 25% AUC,13%SHGUC ,22% HGUC, 2.5% inadequate . The follow up biopsy was as follows: benign 21%(n=25), LGUN 25% (n=30),HGUC 54%(n=65) . Cyto-histo correlations are shown in table 1 and 2.

When comparison was done between the two reporting systems, 25% of cases have been assigned to atypical category by TPS vs 39% when we used the institutional reporting system. Also more cases were diagnosed as negative on cytology (37% vs 27%) using TPS. There is no significant change in SHGUC (suspicious for high grade)/HGUC category using both the systems.

One of the most important findings is the difference in the performance of AUC category using both system - 56% of AUC were subsequently diagnosed as HGUC using TPS whereas it was only 36% using institutional reporting system .In addition to that there are significant differences between predictive values for subsequent HGUC in different categories using both the system. The positive predictive value (PPV) for Inadequate , NHGUC, AUC, SHGUC, HGUC are 33%,18%,57%,87% and 100% respectively using TPS whilst it is 21%,36% ,90%,96% for NM, AUC, SM, PM respectively using the original system of reporting.

Table 1:Correlation between cytology and histology using The Paris System

Histology	Cytology				
	NHGUN (N=45,37%)	ATYPICAL (n=30 ,25%)	SHGUC (n=16, 13%)	HGUC (n=26,22%)	INADEQUATE (n=3,2.5%)
BENIGN	15	7	2	0	1
LGN	22	6	0	0	2
HGUC	8	17	14	26	1
PPV forHGUC	18%	57%	87%	100%	33%

LGN-low grade neoplasm, NHGUN-negative for high frade urothelial neoplasm, HGUC-high grade urothelial carcinoma, SHGUC-suspicious for high grade urothelial carcinoma, PPV-positive predictive value.

Table 2-Correlation between cytology and histology using institutional reporting system

Histology	Cytology			
	NM(n=28,23%)	AUC(AR+AU,n=47,39%)	SM (n=21,17%)	PM (n=24,20%)
BENIGN	10	13	1	1
LGN	12	17	1	0
HGUC	6	17	19	23
PPV for HGUC	21%	36%	90%	96%

NM-negativefor malignancy including inflammatory smear,only degenerated cells,AUC- atypical urothelial cell,AR-atypical favouring a reactive process,AU-atpical cells unclear of whether neoplastic or reactive,SM-suspicious for malignancy,PM-positive for malignancy

DISCUSSION-

TPS has been conceived in 2013 during an international conference of cytology held in Paris with the aim to standardise the reporting of urine cytology .It proposes 7 diagnostic categories with defined cytomorphologic characteristic for each category .(6)

Since then several studies have evaluated its impact on the performance of urine cytology. For example , Wang Y et al has found that rate of atypical category decreased from 18.6% to 14.4% , Concurrently prevalence of benign category increased from 75.4% to 80% using TPS. They found significant difference in the predictive values of AUC and NGHGUC category.(7)

Meilleroux J et al has reported significantly fewer low-grade urothelial neoplasms (0.94% vs 1.84%; P<.05) .More cases of SHGUC were found (2.09% vs 0.73%; P<.01) as compared with before use of TPS. For the AUC category, there was no significant change in frequency noted for before versus after TPS (6.12% vs 5.18%). They also found significantly increased rate of detection of HGUC using TPS .(8)

In a study by Malviya K et al reporting by TPS detected 13% HGUC and 5.1% atypical verses 7.3 % and 11.9% by their original reporting system respectively.(9)

Recently ,Hassan M et al reported that only 26% cases give atypical diagnosis using TPS compared to 37% diagnosed as atypical by previous system .Also the association of AUC with subsequent HGUC on histology increased from 33% to 55% using TPS.(5)

Granados et al found that TPS has higher sensitivity for HGUC than their previous reporting system but using TPS has notably increased atypical category.(10)

The present study demonstrates that implementing TPS has improved overall performance of urine cytology in several aspects. This study has found increasing number of NHGUC and decrease in number of AUC cases ,which is possibly due to application of new strict criteria defined by TPS . The prediction of subsequent HGUC for AUC category significantly increased from 36% to 57% using TPS. This may be explained by the fact that previously we designated a cell atypical simply when its N/C ratio exceeds more than 0.5 .but TPS require additional cytological features like hyperchromasia ,irregular nuclear membrane or clumped chromatin to define a cell as atypical.

CONCLUSION-

The Paris System helps to improve the performance of urine cytology by decreasing cases in AUC category and increasing its prediction of subsequent HGUC .
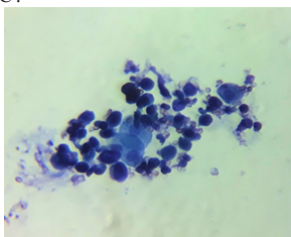

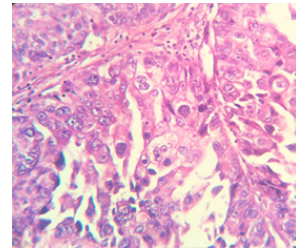**Fig1 – Microghraph shows high grade urothelial carcinoma on cytology .(Pap 40x)**

Fig 2- Micrograph shows histopathological features of high grade urothelial carcinoma from the same case (H &E 40x) .

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